HEPATORENAL SYNDROME

Professor Monir Bahgat

GRADE system

HRS

Professor Monir Bahgat

Grading evidence and recommendations (adapted from the GRADE system)

	Notes	Symbol
Quality of Evidence		
High	Large, high quality randomized control trials. We are confident that the true effect lies close to that of the estimate of the effect.	A
Moderate	Limited or conflicting data from randomized control trials. The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.	B
Low	Observational studies or very small randomized control trials. The true effect may be substantially different from the estimate of the effect.	C
Very low	Expert opinion. The estimate of effect is very uncertain, and often will be far from the truth.	D
Grading Recommendation[a]		
Strong 'We recommend'	Conditions for which there is evidence and/or general agreement that a given procedure or treatment is beneficial, useful and effective	1
Weak 'We suggest'	Conditions for which there is conflicting evidence and/or divergence of opinion about the usefulness/efficacy of a procedure or treatment	2

Introduction

HRS

Definition

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kidney injury resulting from renal vasoconstriction in the setting of systemic & splanchnic arterial vasodilatation in patients with advanced cirrhosis.

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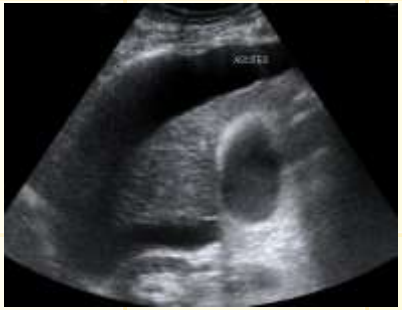

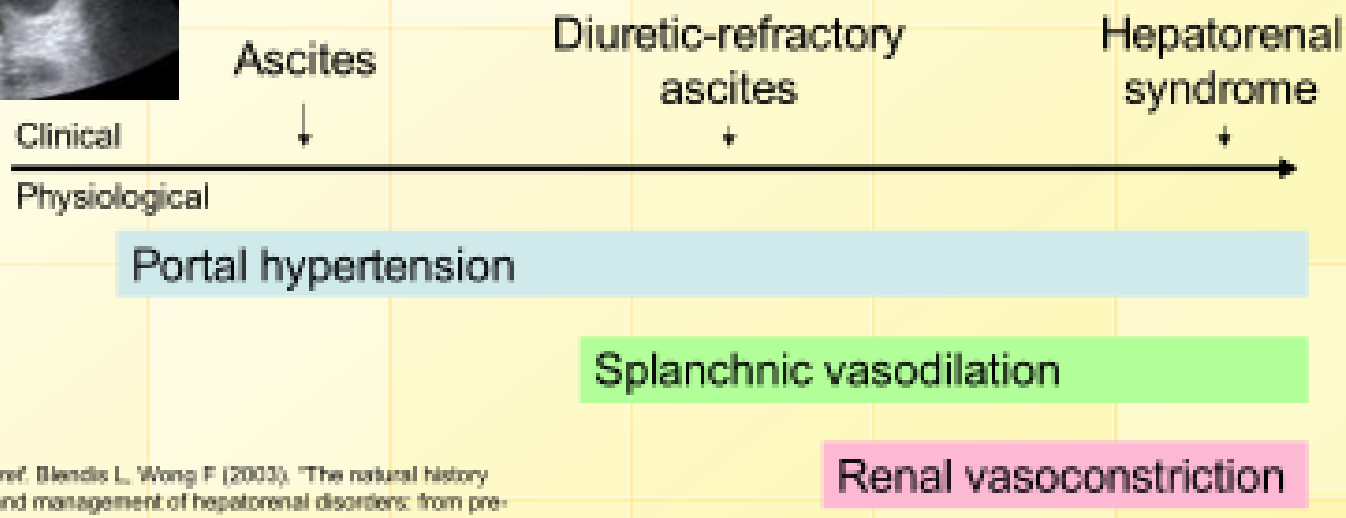

(ref: Blendis L, Wong F (2003). "The natural history and management of hepatorenal disorders: from pre-ascites to hepatorenal syndrome". *Clin Med* **3** (2): 154–9. PMID 12737373.)

Types

Types

HRS is typically subdivided into two types:

- **Type-1:** Rapid deterioration in kidney function with the serum creatinine increasing by >100% from baseline to **>2.5 mg/dl** within a "**two-week"** period.

- **Type-2:** HRS occurs in patients with refractory ascites with either a steady but moderate degree of functional renal failure (≥ 1.5 mg/dl) or a deterioration in kidney function that does not fulfill the criteria for HRS type-1.

Occurrence

Occurrence

In patients with “advanced” cirrhosis, HRS occurs in:

18% within **one year** of diagnosis.

40% at **five** years.

Prognosis

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Untreated, “median survival” is:

Two weeks for patients with **type-1** HRS.

Four - six months in patients with **type-2** HRS.

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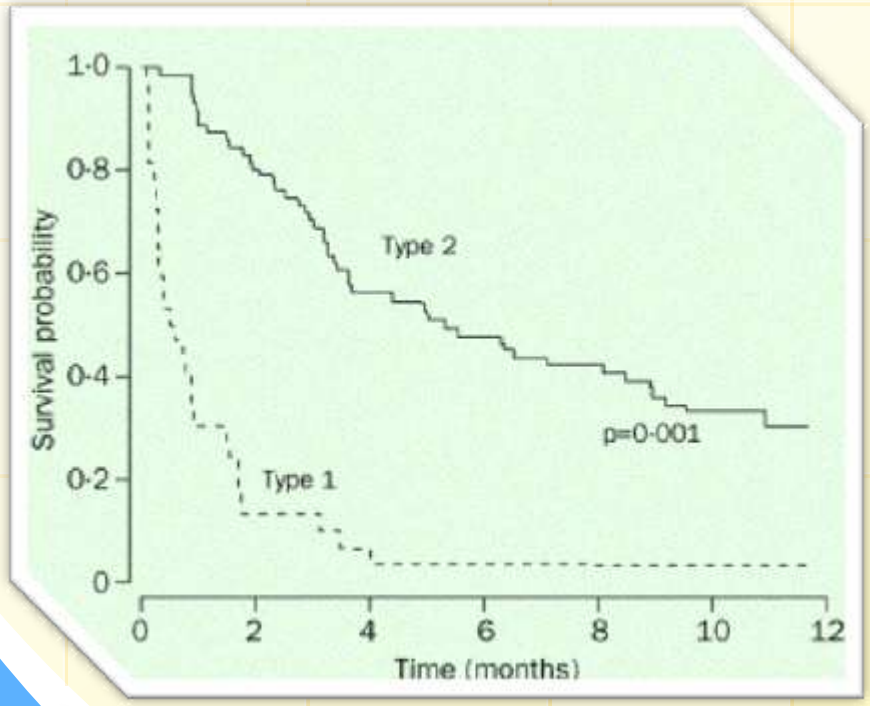

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	Type 1 HRS	Type 2 HRS
Course	Acute (Doubled serum creatinine in <14 days)	Progressive
Triggering event	Present in >50% of patients	Usually absent
Diuretic resistant ascites	Present in <50% of patients	Always present
Prognosis (3-month survival)	20%	40%

Current Vascular Pharmacology, **2014**, *12,* 125-135

Agenda

HRS

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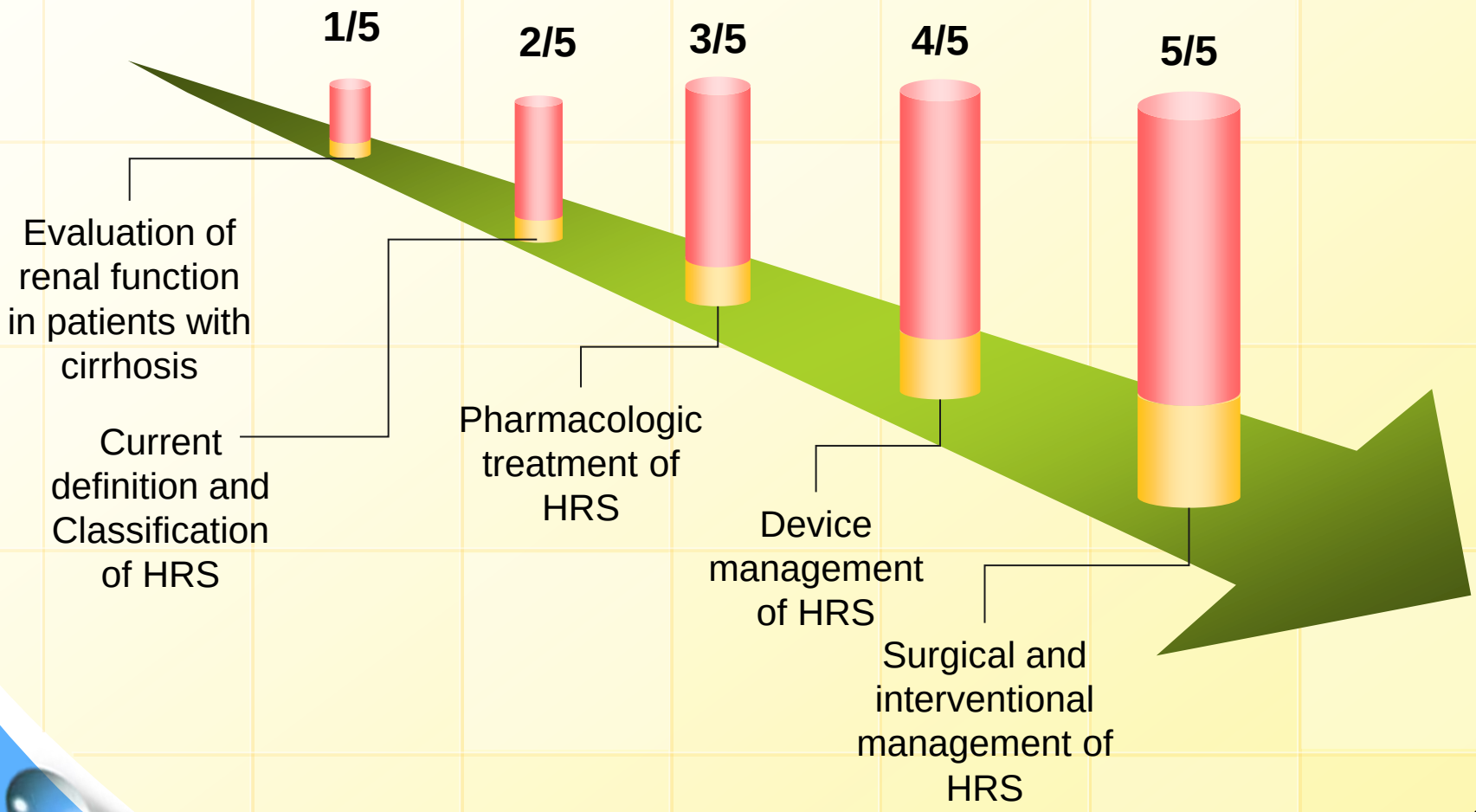
1/5
2/5
3/5
4/5
5/5
Evaluation of renal function in patients with cirrhosis
Current definition and Classification of HRS
Pharmacologic treatment of HRS
Device management of HRS
Surgical and interventional management of HRS

I. Evaluation of renal function in patients with cirrhosis

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1. Serum creatinine measurements should be used to evaluate renal function in patients with advanced cirrhosis until more reliable methods of measuring renal function become generally available (1D).

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Serum cystatin C ????

I. Evaluation of renal function in patients with cirrhosis

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Exogenous clearance markers ???

I. Evaluation of renal function in patients with cirrhosis

2. GFR derived equations should be used cautiously for assessment of kidney function in cirrhosis since they tend to overestimate GFR (2D).

II. Definition and classification of renal impairment in cirrhosis

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1. Classify AKI in the setting of cirrhosis according to RIFLE criteria (Not Graded).

Risk, **I**njury, **F**ailure, **L**oss, **E**ndstage

II. Definition and classification of renal impairment in cirrhosis

ADQI criteria for the definition and classification of AKI (modified RIFLE criteria)

AKI Stage	Serum creatinine criteria	Urine output criteria
1 (Risk)	Increase Scr ≥ 0.3 mg/dL within 48 hours or an increase 150 - 200% (1.5- to 2-fold) from baseline	< 0.5 ml/kg/hour for > 6 hours
2 (Injury)	Increase Scr 200% to 299% (≥ 2- to 3-fold) from baseline	< 0.5 ml/kg/hour for > 12 hours
3 (Failure)	Increase Scr ≥ 300% (≥ 3-fold) from baseline or Scr ≥ 4.0 mg/dL with an acute increase of ≥ 0.5 mg/dL or initiation of renal replacement therapy	< 0.3 ml/kg/hour for 24 hours or anuria for 12 hours

II. Definition and classification of renal impairment in cirrhosis

1996 Criteria

Major Criteria

- Chronic or acute liver disease with advanced hepatic failure and portal hypertension.
- Serum creatinine > 1.5 mg/dL or 24-h creatinine clearance of < 40 mL/min.
- Absence of shock, ongoing bacterial infection, and current or recent treatment with nephrotoxic drugs. Absence of gastrointestinal fluid losses (repeated vomiting or intense diarrhea) or renal fluid losses
- No sustained improvement in renal function defined as a decrease in serum creatinine to < 1.5 mg/dL or increase in creatinine clearance to 40 mL/min or more following diuretic withdrawal and expansion of plasma volume with 1.5 L of isotonic saline.
- Proteinuria < 500 mg/dL and no ultrasonographic evidence of obstructive uropathy or parenchymal renal disease.

Minor Criteria

- Urine volume < 500 mL/d
- Urine sodium < 10 mEq/L
- Urine osmolality > plasma osmolality
- Urine red blood cells < 50 per high power field

2007 Criteria

- Cirrhosis with ascites
- Serum creatinine > 1.5 mg/dL
- No improvement of serum creatinine (decrease to a level ≤ 1.5 mg/dL) after at least two days of diuretic withdrawal and volume expansion with albumin. The recommended dose of albumin is 1 g/kg of body weight per day up to a maximum of 100 g/day
- Absence of shock
- No current or recent treatment with nephrotoxic drugs
- Absence of parenchymal kidney disease as indicated by proteinuria > 500 mg/day, microhematuria (> 50 red blood cells per high power field), and/or abnormal renal ultrasonography

II. Definition and classification of renal impairment in cirrhosis

2. Classify CKD in the setting of cirrhosis according to Kidney Disease Outcomes Quality Initiatives (K/DOQI) (Not Graded).

II. Definition and classification of renal impairment in cirrhosis

3. Acute on CKD in cirrhosis is defined as a rise in SCr ≥ 0.3 mg/dL in <48 hours or an increase in SCr ≥ 50% from baseline, or in a patient with cirrhosis whose baseline GFR has been <60 ml/min calculated with the MDRD-6 formula for >3 months (Not Graded).

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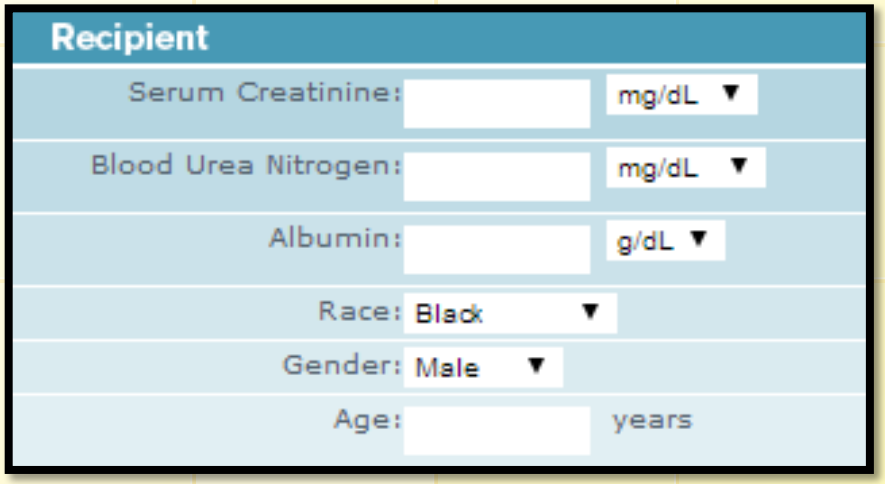

http://www.transplantcalculator.com/Renal-Function-Calculators/GFR-by-exMDRD.aspx

II. Definition and classification of renal impairment in cirrhosis

Diagnosis	Definition
Acute Kidney Injury	• A rise in Scr ≥ 50% from baseline, or a rise Scr > 0.3 mg/dL • Type-1 HRS is a specific form of acute kidney injury
Chronic Kidney Disease	• GFR < 60 ml/min for > 3 month calculated using MDRD-6 formula
Acute on Chronic Kidney Disease	• Rise in Scr ≥ 50% from baseline or a rise of Scr > 0.3 mg/dL in a patient with cirrhosis whose GFR is < 60 ml/min for > 3 month calculated using MDRD-6 formula

III. Pharmacologic treatment of HRS

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1. Use hemodynamic monitoring, when possible:
   to help with management of fluid balance (2D).

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2. Optimally resuscitate patients with type-1 HRS with *albumin + a vasoconstrictor* (1A), preferentially terlipressin (2C):

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2. Optimally resuscitate patients with type-1 HRS with *albumin + a vasoconstrictor* (1A), preferentially terlipressin (2C):

Albumin: *1* g/kg for two days (maximum 100 g/d), followed by 20 to 40 g/d.

Terlipressin: 0.5 – 2 mg IV every 4 – 6 hours with stepwise dose increments every few days if there is no improvement in serum creatinine (maximum 12 mg/d if no S/E).

Maximum treatment: 14 days.

III. Pharmacologic treatment of HRS

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If terlipressin is unavailable, alternative vasoconstrictors such as a combination of octreotide and midodrine, together with albumin should be considered.

III. Pharmacologic treatment of HRS

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If terlipressin is unavailable, alternative vasoconstrictors such as a combination of octreotide and midodrine, together with albumin should be considered.

Midodrine: 7.5 to 12.5 mg orally three times. Titrate to achieve a 15 mm Hg increase in MAP from baseline.

Octreotide: 100 to 200 µg subcutaneously three times daily or 25 µg bolus, followed by intravenous infusion of 25 µg/ hour

IV. Device management of HRS

IV. Device management of HRS

1. Withhold renal replacement therapy (RRT) in patients with decompensation of cirrhosis who are not candidates for liver transplantation (1D).

IV. Device management of HRS

2. **“Artificial liver support therapies”** for HRS should be limited to research protocols (2D).

IV. Device management of HRS

	Technique
Artificial (Non-cell based)	
Hemoperfusion	Removal of protein-bound toxins by circulating blood over a sorbent material
Hemodiabsorption	Hybrid process in which blood is passed through a hemodialyzer containing a suspension of sorbent material, such as charcoal or resin, in the extracapillary space
Plasma Exchange	Exchange of plasma volume
Plasmapheresis	Plasma is separated from the cellular blood components and replaced with normal plasma constituents, allowing the removal of circulating toxins and waste products.
Plasma Filtration	Removes a specific plasma fraction containing substances within a specific molecular weight.
Albumin dialysis	Albumin containing dialysate using an anion exchange resin and active charcoal adsorption allowing albumin-bound toxins in the blood to cross the membrane and bind to the albumin. Water soluble toxins are dialyzed from the albumin circuit by a standard hemodialysis or continuous renal replacement therapy (CRRT) machine.
• Single Pass Albumin Dialysis (SPAD)	
• Prometheus	
• Molecular Adsorbent Recirculating System (MARS)	
Bioartificial (Cell-based)	
Porcine	
• HepatAssist • Bioartificial Liver Support System (BLSS) • Modular Extracorporeal Liver Support (MELS) • Hybrid-Bioartificial Liver (HBAL) • Radial Flow Bioreactor (RFB) • TECA-Hybrid Artificial Liver Support System • AMC-Bioartificial Liver	
Human	
• Extracorporeal Liver Assist Device (ELAD)	

V. Interventional & Surgical management of HRS

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1. Use a transjugular intrahepatic portosystemic shunt (TIPS) as a treatment option for patients with type-2 HRS with refractory ascites who require large volume paracentesis (1C).

V. Interventional & Surgical management of HRS

2. Liver transplantation alone for candidates with type-1 HRS for less than four weeks AND simultaneous liver kidney for those at risk for non-recovery of renal function (2D).

Thank You!

Professor Monir Bahgat